Synthesis of TP-2758

**Significance:** TP-2758 is in development for the treatment of complicated urinary tract infections caused by Gram-negative pathogens. The closing stage of the synthesis depicted features the installation of the chiral pyrrolidine moiety in fragment G using Ellman’s chiral sulfinamide auxiliary B (99% ee). The conjunction of complex fragments G and H using chemistry developed by Myers and coworkers (J. Am. Chem. Soc. 2008, 130, 17913) delivered the advanced intermediate I in 89% yield.

**Comment:** Enantioselective deprotonation of N-Boc pyrrolidine using s-BuLi and (-)-sparteine afforded the lithium reagent (S)-K that participated in a palladium-catalyzed Negishi coupling with bromoarene J to give enantioenriched pyrrolidine (R)-L in 63% yield (>90% ee). By using diamine (S,S)-M as a (+)-sparteine surrogate, the corresponding Negishi reaction delivered (S)-L in 50% yield (93% ee). Neither of these alternatives was robust, and the yields could not be improved.

SYNFACTS Contributors: Philip Kocienski

Synfacts 2016, 12(5), 0439 | Published online: 18.04.2016
DOI: 10.1055/s-0035-1561984 | Reg-No.: K02016SF